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Acupuncture for treating overactive bladder in adults (Protocol)

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[Intervention Protocol]

Acupuncture for treating overactive bladder in adults

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effects of acupuncture for treating OAB in adults; and summarise the principal findings of relevant economic evaluations.

BACKGROUND

For a glossary of terms used, see Appendix 1.

Description of the condition

Overactive bladder (OAB) is defined by the International Continence Society as "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology" (Abrams 2017). OAB can be further categorised into "OAB-dry" (where urinary incontinence is absent) and "OAB-wet" (where urinary incontinence is present) (Abrams 2017). Abrams 2012 reported that urinary frequency accompanies OAB in 20% to 25% of cases, and nocturia in 70% to 75% of cases. Around one in three people with OAB also experience urinary incontinence (Irwin 2006).

OAB is common. An epidemiological study, the EPIC study, was conducted in five countries (Canada, Sweden, Italy, Germany, and the UK) and included 19,165 participants (Irwin 2006). It reported 11.8% of the population had OAB symptoms, with slightly more women affected (12.8%) than men (10.8%) (Irwin 2006). This is equivalent to one in nine of the general adult population (Irwin 2006). The prevalence of OAB increases with age and symptoms are reported to occur in 40% of men and 46% of women aged 65 years or over (Sexton 2011).

The exact pathophysiology underlying OAB is not fully understood and it is thought that several processes may contribute to developing symptoms (Malde 2018). These processes include: abnormal secretion of acetylcholine during bladder filling, which may result in afferent activation; compounds released by urothelial cells, which may affect cell signalling; alteration in smooth muscle properties; abnormal afferent activity resulting in increased efferent responses, which compromises voluntary bladder control; and altered cognitive responses, specifically in the orbitofrontal cortex.

OAB is most often present when there is no underlying neurological disease; this is known as idiopathic OAB. However, it is also sometimes associated with neurological conditions, including stroke, Parkinson's disease, multiple sclerosis, and spinal cord injury. People presenting with OAB should be screened to rule out neurological causes (Tse 2016).

OAB is a long-term condition that reduces quality of life, leading to increased anxiety and depression and a negative effect on self-esteem (Lai 2016; Tubaro 2004; Wein 2009). Ou 2019 reported that people with lower urinary tract symptoms (LUTS) and depression are at a greater risk of developing dementia. In a survey conducted in 2017 (Rantell 2017), 88% of participants reported experiencing symptoms for over 10 years. Participants reported negative effects on physical, social, domestic, occupational, and sexual domains.

Given the high prevalence of OAB, treatment costs are significant. The National Overactive Bladder Evaluation Programme (NOBLE) cited the cost of treating OAB in the USA in 2000 was USD 12.02 billion (Hu 2003). A further study estimated that the cost of providing care would rise with an aging population; projected costs for 2020 are USD 82.6 billion per annum (Ganz 2010).

OAB is usually diagnosed by a thorough history and physical examination. Validated symptom questionnaires are used to document and quantify symptoms, while clinical examination can help exclude other causes of LUTS. A bladder diary can assess the frequency and severity of symptoms (NICE 2019).

Description of the intervention

Initial treatment for OAB includes lifestyle modification, pelvic floor exercises, and fluid management. Where these are unsuccessful, people are offered anticholinergic drugs or β3-adrenoreceptor agonists. If medications do not control symptoms, then surgical interventions may be required. Surgical treatment for OAB includes intravesical botulinum toxin injection, sacral neuromodulation, augmentation cystoplasty, and urinary diversion (NICE 2019). Although acupuncture is not currently offered universally as a treatment for OAB, there is a growing body of literature that reports positive outcomes when using this modality to treat the symptoms of OAB (Aydoğmuş 2014; Yuan 2015; Zhao 2018).

Acupuncture refers to the practice of inserting multiple fine needles throughout the body in order to achieve a positive physiological response (White 2009). Needling can be performed within the dermatome of the affected area; at prominent acupoints found throughout the body which, according to Traditional Chinese Medicine (TCM) theory, have specific effects on symptoms; on the visible part of the ear (the auricle); and with the addition of electrical stimulation (electroacupuncture).

Acupuncture is practised widely throughout Asia, Europe, and Northern America and has a low adverse event risk profile, with the most common adverse events being reported as transient (Clarkson 2015; MacPherson 2001). Examples of adverse events reported in the literature include bleeding at the site of needle insertion, pain at the site of the inserted needle, or an initial increase in pain at the site of injury (Witt 2009).

A typical acupuncture session may last between 15 to 40 minutes. Needles may be stimulated, either manually by the clinician (needles turned in the acupoint) periodically throughout the session, or continually through an electroacupuncture device that delivers an electrical current. The frequency and duration of treatment may vary depending on clinician preference and patient response.

How the intervention might work

While the exact mechanism of how acupuncture treats OAB remains unclear, several theories exist. Sensory information from afferent nerves from the pelvic, pudendal, and hypogastric nerve roots directly relate to the lower urinary tract (Pullman 2016). Needling within the skin and muscles that these nerves supply may reduce OAB through inhibition of peripheral nerves (Hino 2010), via brain areas that control bladder activity (Wang 2012). Furthermore, the Brain Bladder Control Matrix, where the periaqueductal gray, limbic system, and prefrontal cortex are believed to have a large influence upon the bladder's function, have been found to alter during and after a course of acupuncture (Dhond 2008; Huang 2012). This infers that the beneficial effects of acupuncture on OAB symptoms could be partially explained through signalling changes from the central nervous system to the bladder. Acupuncture has been shown to exert an effect on the autonomic nervous system (Napadow 2013), further endorsing the view that acupuncture can influence the human nervous system and therefore may affect symptoms arising from a disturbance in this system.

In TCM theory, the maintenance of health and well-being is dependent upon the quality of energy (Qi), which emanates from the visceral organs. When Qi becomes unbalanced, symptoms of ill health occur. In the case of OAB, this would be attributable to deficient kidney and bladder Qi (Maciocia 2008). Acupoints on the bladder, kidney, and spleen meridians are believed in TCM theory to directly benefit urinary symptoms by restoring Qi balance (Maciocia 2008). There is debate between acupuncture practitioners regarding the concepts described and further high-quality research is required to explore the putative mechanisms underpinning the observed effects of acupuncture.

Why it is important to do this review

There are specific concerns and side-effects linked to some treatments for OAB. The additive effect of anticholingeric medications may be linked to the development of dementia (Gray 2015). Surgical treatments are invasive, may be contraindicated, or carry a significant risk in older people who are more likely to have co-morbidities. Surgical interventions have a significantly higher risk profile and recovery period when compared to acupuncture (NICE 2019; Witt 2009). In light of this, it is important to investigate alternative strategies for managing OAB.

Published Cochrane Reviews concerning treating OAB include: anticholinergics (Madhuvrata 2012), implanted sacral neuromodulation (Herbison 2009), onabotulinumtoxin A (Duthie 2011), and bladder training (Wallace 2004). Currently, the role of acupuncture in the treatment of OAB has not been assessed in a Cochrane Review. The efficacy of acupuncture is uncertain, there is no consensus with regard to treatment protocols, and it is anticipated that some of the research available may be of poor quality (Forde 2016). High-quality evidence is essential to allow patients to make fully informed decisions regarding their choice of therapies, and this Cochrane Review may highlight the need for more high-quality research into acupuncture for OAB.

OBJECTIVES

To assess the effects of acupuncture for treating OAB in adults; and summarise the principal findings of relevant economic evaluations.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs), quasi-RCTs, and cross-over studies of acupuncture for treating OAB in adults. By quasi-RCTs, we mean trials in which randomisation may be predictable, such as the allocation of participants by day of the week, date of birth, or sequence of entry into the trial.

Types of participants

We will include studies of adults aged over 18 years with a diagnosis of OAB that fits the criteria defined by the International Continence Society as "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology" (Abrams 2017).

This review is addressing treatment for idiopathic OAB and we will therefore exclude participants who have OAB symptoms that are a manifestation of a neurological condition (e.g. multiple sclerosis, Parkinson's disease, and stroke).

Types of interventions

We will include studies of acupuncture interventions intended to treat the symptoms of OAB that involve needle insertion at defined acupuncture points. This includes body acupuncture, scalp acupuncture, auricular acupuncture, and electro-acupuncture. We will seek clarification from study authors if the type of acupuncture used in a study is not clear.

Sham acupuncture is designed to assist with blinding participants about the type of treatment they are receiving. It can be delivered using a needle which appears to pierce the skin but does not, or by inserting needles at non-acupuncture points.

We will include the following comparators.

- Acupuncture versus no treatment
- Acupuncture versus sham acupuncture
- Acupuncture versus conservative treatments (including bladder retraining, fluid management, pelvic floor rehabilitation, weight loss, and smoking cessation)
- Acupuncture versus medication for OAB

We believe that the comparisons of particular interest to patients and practitioners are acupuncture versus no treatment or sham acupuncture, and acupuncture versus medication for symptoms of OAB.

Types of outcome measures

Primary outcomes

- Number of participants whose OAB symptoms were cured or improved (assessed using validated urinary symptom and incontinence-specific patient-reported outcome measures (i.e. the Bristol Female Lower Urinary Tract Symptoms questionnaire (BFLUTS) (Hiller 2002), International Consultation on Incontinence Questionnaire-Urinary Incontinence (ICIQ-UI) (Avery 2004), three-day bladder diaries (Jimenez-Cidre 2015). Numbers of participants defined as cured in studies will be reported. Where cure rates are not used, we will use symptom improvement rates)
- Number of major adverse events (i.e. death, serious infection from needle insertion, pneumothorax from needle insertion, any complication resulting in hospitalisation as an inpatient or an outpatient)
- Number of minor adverse events (i.e. fainting, vomiting, pain on needle insertion, bleeding on needle removal, bruising, and fatigue)

Secondary outcomes

- Presence or absence of urinary urgency (measured by patient-reported outcomes)
- Daytime urinary frequency (i.e. number of voids during waking hours measured by patient-reported outcomes)
- Episodes of urinary incontinence in a 24-hour period (measured by patient-reported outcomes)
- Episodes of nocturia (i.e. number of voids after going to sleep and prior to waking measured by patient-reported outcomes)

- Improvement in objective measures of urinary incontinence (i.e. urodynamic testing parameters)
- Improvement in general quality of life (assessed using validated scores i.e. EQ-5D (Rabin 2001), medical outcomes SF-36 (Ware 1992), ICEpop CAPability measure for Adults (ICECAP A) (Al-Janabi 2013)

Timing of outcome assessment

We will include outcome measures that are applied as follows.

- Within three weeks of randomisation (baseline measurement)
- Within 12 weeks of commencing treatment (short-term outcomes)
- Longer than 12 weeks after commencing treatment (long-term outcomes)

Acupuncture treatments for OAB symptoms are usually applied on at least a weekly basis. Studies vary in the number of treatments given, with usual practice between 4 to 12 treatments. Acupuncture is thought to have a carryover treatment effect and so the measurement of long-term outcomes is of interest in this review.

Main outcomes for 'Summary of findings' tables

- Number of participants whose OAB symptoms were cured or improved
- Number of major adverse events
- Number of minor adverse events
- Presence or absence of urinary urgency
- Daytime urinary frequency
- Episodes of urinary incontinence in a 24 hour period
- Episodes of nocturia (i.e. number of voids after going to sleep and prior to waking)

Where not otherwise indicated, all outcomes for the 'Summary of findings' tables will be measured within 12 weeks of commencing treatment (i.e. short-term).

Search methods for identification of studies

We will not impose any language or other limitations on any of the searches described below.

Electronic searches

Search for clinical effectiveness studies

This review will draw on the search strategy developed for Cochrane Incontinence. We will identify relevant trials from the Cochrane Incontinence Specialised Register. For more details of the search methods used to build the Specialised Register, please see the Group's webpages where details of the Register's development (from inception) and the most recent searches performed to populate the Register can be found. To summarise, the Register contains trials identified from the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, ClinicalTrials.gov, WHO ICTRP, NIHR Be Part of Research and handsearching of journals and conference proceedings. Many of the trials in the Cochrane Incontinence Specialised Register are also contained in CENTRAL.

The terms that we will use to search the Cochrane Incontinence Specialised Register are given in Appendix 2.

We will also search the Allied and Complementary Medicine database (AMED) on OvidSP.

In addition, electronic bibliographic databases where knowledge of the Chinese language is necessary will be searched.

- China National Knowledge Infrastructure (CNKI)
- Chinese Medical Literature Database (CBM)
- Chinese Medical Current Content (CMCC)
- VIP, and
- WANFANG (China Online Journals)

Search for economic evaluations

We will perform additional searches for the brief economic commentary (BEC). We will search the:

- NHS Economic Evaluation Database (EED) on the UK Centre for Reviews and Dissemination (CRD) website (covering from the earliest record in NHS EED, dating from 1968, up to and including 31 December 2014 when their coverage ended)

As NHS EED is no longer actively updated, we will perform additional searches of the following databases to identify eligible studies added to these databases from 1 January 2015 onwards:

- MEDLINE on OvidSP (covering 1 January 1946 to the most recent available version); and
- Embase (on OvidSP) (covering 1 January 1974 to the most recent available version).

Details of the searches that will be performed can be found in Appendix 3.

Searching other resources

We will search the reference lists of relevant articles and will use these to identify economic evaluation studies. For the economic evaluations included in the BEC, we will perform forward citation searching.

Data collection and analysis

We will conduct data collection and analysis in accordance with methods specified in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019).

Selection of studies

As we anticipate that a proportion of studies will be available only in Mandarin, four review authors will form pairs to select studies and extract data (EH and CC for English-language studies; and YYZ and one other (to be recruited) for Mandarin-language studies). Both pairs of review authors will use the same software, and screening and data extraction processes.

Using Covidence, the above pairs of review authors will independently screen the titles and abstracts identified by the search. We will obtain the full text of potentially relevant reports and assess these against the review's inclusion criteria. Review authors will compare and discuss their results, and will resolve disagreements by consulting a third review author (KB).

Data extraction and management

Using Covidence, the above pairs of review authors will independently extract the data from selected studies. We will compare and discuss data extraction forms for each study. A third review author (GB) will resolve any disagreements.

Assessment of risk of bias in included studies

We will use Cochrane's 'Risk of bias' tool to assess the risk of bias in included studies (Higgins 2011). The above pairs of review authors will individually assess each of the identified studies against the six domains (sequence generation, allocation concealment, blinding of participants and study personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and any other source of potential bias). For each domain, we will rate the study as either at 'high', 'low', or 'unclear' risk of bias. A third review author (KB) will arbitrate any disagreements.

Measures of treatment effect

We will use Review Manager 5 (RevMan 5) to perform statistical analysis of the data collected from selected studies (Review Manager 2014). One review author (EH) will be responsible for data entry into RevMan 5 and a second review author (CC) will check the process.

For dichotomous outcome data, we will measure the treatment effect using risk ratios (RR) with 95% confidence intervals (CIs). For continuous outcome data, we will use mean difference (MD) values with 95% CIs to measure the treatment effect. If the studies identified use differing scales to measure the same outcome, it may be necessary to use the standardised mean difference (SMD) with 95% CIs.

Unit of analysis issues

We intend to include studies using a cross-over design if they meet the inclusion criteria and will apply the guidance of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019). The risk of bias assessment will pay particular attention to the dropout rate following first treatment, the randomisation process to first treatment, and the reporting of these events. If the dropout rate following the first treatment is high and the study reports first treatment only data, we will exclude these studies. An assessment of the effect of carryover from treatment one to treatment two will be made and, if it is felt that the treatment carryover would significantly affect reported results, these studies will be excluded from the review.

If insufficient detail is reported in studies to make the judgements described above, we will contact study authors in order to obtain the details required.

If there is a group of cross-over studies reporting the results of a paired analysis (i.e. as a MD), we could use the generic inverse-variance method (GIV) to perform a meta-analysis or meta regression as required.

Dealing with missing data

We will include studies reporting results using an intention-to-treat (ITT) analysis if the participants were analysed in the trial arm to which they were originally assigned. If this information is not clear from the trial report, we will contact study authors for clarification.

If there are missing data reported that could be calculated using recognised statistical methods, we will perform these calculations. The conventional analysis of meta-analysis will be used if only individuals with available data are adequate and when we are confident that the data are missing at random (MAR) in every study (i.e. that the probability of missing data does not depend on unobserved outcomes, conditional on observed variables).

However, if data are not missing at random, we will use two methods based on plausible assumptions about the missing data. We will impute missing values based on the distribution of reasons for missing data. After specifying the magnitude and uncertainty of possible departures from the missing at random assumption, we will use these to correct bias and re-weight the studies by employing a pattern mixture model and describing how the outcome in the missing participants is related to the outcome in the completers. This relationship will be informed using expert opinion in the review author team.

Assessment of heterogeneity

We will assess the heterogeneity of studies by visually assessing funnel plots and calculating the Chi^2 and I^2 statistics using RevMan 5 software (Review Manager 2014). This data will allow us to assess heterogeneity and decide whether a meaningful meta-analysis can be performed. The assessment of heterogeneity will be guided by the *Cochrane Handbook for Systematic Reviews of Interventions* as follows (Higgins 2019):

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

Assessment of reporting biases

If sufficient studies are identified, we will produce a funnel plot to explore publication bias.

Data synthesis

We will synthesise data collected using RevMan 5 (Review Manager 2014). We will generate forest plots and 95% CIs for each outcome and will use a fixed-effect model. However, if the data are heterogeneous, we will use a random-effects model. A meta-analysis may not be possible if data is sparse and the level of heterogeneity is very high. In this instance, we will undertake a narrative synthesis of the results.

Subgroup analysis and investigation of heterogeneity

If the data allows, we will perform the following subgroup analyses.

- Sex (male versus female)
- Form of acupuncture (body acupuncture versus electroacupuncture versus auricular)
- Age (under 65 years versus over 65 years)

Sensitivity analysis

If the eligibility of some included studies is dubious (i.e. if they have missing data), it may be necessary to perform a sensitivity analysis to assess the robustness of the results. We will complete this at the end of the data analysis process if indicated for studies with a high risk of bias.

If the data allows, we will also perform a cumulative meta-analysis using Stata software (Stata 2019), where studies are added one at a time in a specified order according to date of publication or quality to check the contribution of added studies.

Summarising findings and assessing certainty of the evidence

We will use the GRADE approach to assess the certainty of evidence related to the 'Main outcomes for 'Summary of findings' tables' as listed in the Types of outcome measures (Schünemann 2019). We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias). We will justify all decisions to downgrade the certainty of studies using footnotes. Two review authors will undertake this work (EH and GB).

We will prepare 'Summary of findings' tables using the GRADEpro software for the main comparisons pre-stated in the Types of interventions if there is sufficient evidence (GRADEpro GDT).

Incorporating economics evidence

Following the search outlined in the Search methods for identification of studies, we will develop a BEC to summarise the availability and principal findings of the full economic evaluations that compare acupuncture with other treatments (Shemilt 2019). This BEC will encompass full economic evaluations (i.e. cost-effectiveness analyses, cost-utility analyses, and cost-benefit analyses) conducted as part of a single empirical study, such as a RCT, a model based on a single such study, or a model based on several such studies.

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APPENDICES

Appendix 1. Glossary of terms

Acetylcholine: a substance that transmits nerve impulses within the central and peripheral nervous systems.

Acupuncture: a treatment derived from ancient Chinese medicine. Fine needles are inserted at certain sites in the body for therapeutic or preventative purposes.

Acupuncture point: a point of the body where an acupuncture needle may be inserted. Acupuncture points are identified by anatomical landmarks and palpation.

Acupoint: a shorthand way of referring to an acupuncture point.

Afferent nerve: a nerve that bring information from the body to the brain.

Anticholingeric: a substance that blocks the action of the neurotransmitter acetylcholine at synapses in the central and the peripheral nervous system. Medications used to treat symptoms of overactive bladder (OAB) include anticholinergic agents.

Augmentation cystoplasty: a procedure that involves making the bladder bigger by adding a piece of tissue from the intestine into the bladder wall. This may improve the ability of the bladder to store urine. It is rarely performed for symptoms of OAB and is viewed as a treatment of last resort.

Bladder Brain Control matrix: the complex nerve pathways governing bladder function.

Bladder retraining: the first-line treatment for urinary symptoms associated with OAB. It involves teaching the bladder to hold more urine and helps to reduce urinary frequency.

β3-adrenoreceptor agonists: a medication that relaxes smooth muscle and so can have a beneficial effect on OAB symptoms.

Co-morbidities: the presence of one or more additional conditions co-occurring with a primary condition.

Dermatome: an area of sensory nerves near the skin that are supplied by a specific spinal nerve root. The body can be divided into regions that are mainly supplied by a single spinal nerve. Dermatomes are named according to their spinal nerve root.

Economic evaluation: the application of analytical methods to identify measure and value both the costs and benefits of alternative interventions in order to provide evidence regarding technical or allocative efficiency and aid decision making for resource allocation (definition taken from the Campbell and Cochrane Economics Methods Group's Glossary) .

Efferent nerve: a nerve that brings information from the brain to the body.

Electroacupuncture: an acupuncture technique that applies small electrical currents to needles that have been inserted at specific points on the body.

Intravesical botulinum toxin injection: a form of treatment where botulinum toxin is injected into the smooth muscle of the bladder wall (the detrusor muscle) in order to treat symptoms of OAB.

Limbic system: interconnected structures in the midline of the brain involved with emotion, memory and regulatory systems.

Meridians: a concept in Traditional Chinese Medicine (TCM) about a path through which the life-energy known as "Qi" flows.

Nocturia: the number of times urine is passed during the main sleep period.

Overactive bladder (OAB): a group of symptoms affecting the urinary system that includes urinary urgency (a sudden and intense desire to pass urine that is hard to defer), frequency (passing urine more frequently than 5 to 8 times in a 24-hour period), nocturia (waking to pass urine at night), urinary incontinence (involuntary passing urine).

OAB-dry: OAB symptoms without urinary incontinence.

OAB-wet: OAB symptoms with urinary incontinence.

Orbitofrontal cortex: a region in the frontal lobes of the brain that is involved in the cognitive process of decision-making.

Pre-frontal cortex: the anterior part of the frontal lobe of the brain, which is highly developed in humans and concerned with complex cognitive, emotional, and behavioural functions.

Peri-aqueductal gray (PAG): a mid-brain structure that plays a critical role in autonomic function and behavioural responses to threatening stimuli.

Qi: believed to be a vital force forming part of any living entity in TCM.

Traditional Chinese Medicine (TCM): a system of medicine traditionally practised in China; acupuncture is one component of this system.

Sacral neuromodulation: a form of treatment where a small nerve stimulator device is implanted in the body to provide stimulation to the sacral nerves. This stimulation is thought to have an effect on the nerves passing between the bladder and the brain and relieve the symptoms of OAB.

Smooth muscle: a type of muscle tissue that contracts without conscious control. The detrusor muscle that forms the bladder wall is made of smooth muscle.

Urinary diversion: a procedure where the tubes that lead from the kidneys to the bladder (ureters) are redirected to outside of the body. The urine is then collected directly without it flowing into the bladder. Urinary diversion is only performed if other treatments have been unsuccessful or are unsuitable.

Urinary incontinence (UI): involuntary passing of urine.

Urothelial cells: the cells that form the lining of the bladder.

Appendix 2. Search of the Cochrane Incontinence Specialised Register

The search terms that will be used to search the Cochrane Incontinence Specialised Register are given below:

((design.cct*) OR (design.rct*))
AND
((topic.urine.incon*) OR (topic.urine.overactive*))
AND
(intvent.phys.acupuncture*)

All searches will be of the keywords field of EndNote (EndNote 2018).

Appendix 3. Search methods for the brief economic commentary (BEC)

We will perform electronic searches designed to identify published reports of relevant economic evaluations to inform the BEC (see 'Incorporating economic evidence' in the Methods). We will search the:

- NHS Economic Evaluation Database (EED) on the UK Centre for Reviews and Dissemination (CRD) website (covering from the earliest record in NHS EED, dating from 1968, up to and including 31 December 2014 when their coverage ended)

As the NHS EED is no longer actively updated, we will perform additional searches of the following databases to identify eligible studies added to these databases from 1 January 2015 onwards:

- MEDLINE on OvidSP (covering 1 January 1946 to the most recent available version); and
- Embase (on OvidSP) (covering 1 January 1974 to the most recent available version).

The economic evaluation search filters which will be applied to our MEDLINE and Embase search strategies will be those formerly used by the CRD to identify published reports of full economic evaluations for indexing on NHS EED. These economic evaluation search filters remain freely available on the CRD Database search strategies webpage (CRD 2015). The other search lines in the MEDLINE and Embase search strategies will be adapted from the electronic search strategies run for our Cochrane Incontinence Specialised Register, along with additional terms for this population developed specifically for this Cochrane Review. Similarly, our NHS EED search strategy will be adapted from search strategies run for our Specialised Register and based on textword and MeSH terms (capturing relevant P-I-C concepts) used to identify eligible studies of intervention effects. We will follow the current economic methods guidance (Shemilt 2019).

CONTRIBUTIONS OF AUTHORS

EH: contributed to working group discussions to shape the idea; developed and wrote the protocol; co-ordinated the review team; and liaised with the Cochrane Incontinence editorial team.
KB: contributed to working group discussions to shape the idea; provided expertise on ageing population and the impact of living with long-term health conditions; and provided general advice for the protocol.
GB: advised on methodology; and provided general advice for the protocol.
CH: contributed to working group discussions to shape the idea; co-wrote the Background section, provided urology expertise and advised on methodology; and provided general advice for the protocol.
YYZ: co-wrote the data collection section; and provided Chinese literature expertise.
NBK: co-wrote the data collection and analysis section; and provided statistical expertise.
CEC: contributed to working group discussions to shape the idea; co-wrote the Background section, provided acupuncture expertise and advised on methodology; and provided general advice for the protocol.

DECLARATIONS OF INTEREST

In accordance with Cochrane's Commercial Sponsorship Policy, the following declarations are applicable for the three years prior to the publication date of this protocol.

EH: none known.
KB: none known.
GB: none known.
CH: Allergan Consultant Speaker Honorarium, Medtronic Speaker Honorarium, Proctor Astellas Speaker Honorarium (none of which concern acupuncture in people with OAB).
YYZ: none known.
NBK: none known.
CEC: none known.

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